

Emergency Use Instructions for Healthcare Providers: Pfizer-BioNTech COVID-19 vaccine for Additional Primary and Booster Doses in Certain Persons Who Completed Primary Vaccination with Vaccines Not Approved/Authorized in the United States

The Centers for Disease Control and Prevention (CDC) is issuing Emergency Use Instructions (EUI) to provide information about the use of the formulation of the COVID-19 vaccine by Pfizer-BioNTech which is approved (licensed) by the Food and Drug Administration (FDA) for the prevention of COVID-19 in individuals 16 years of age and older.¹ These EUI provide information about the use of the COVID-19 vaccine by Pfizer-BioNTech as an additional primary dose in certain immunocompromised persons aged ≥ 12 years and as a booster dose in certain adults aged ≥ 18 years after completion of primary vaccination with certain **non-FDA authorized or approved** COVID-19 vaccines².

These EUI for healthcare providers contain key information regarding the COVID-19 vaccine by Pfizer-BioNTech specific to this use. For additional information about the COVID-19 vaccine by Pfizer-BioNTech COVID-19, refer to the [Comirnaty](#) package insert or the [Full Emergency Use Authorization \(EUA\) Prescribing Information](#). Refer to CDC's [Interim Clinical Considerations](#) for detailed recommendations on use of this vaccine under the EUI; relevant information is contained under the headings "People who received COVID-19 vaccine outside the United States" and "People who received COVID-19 vaccine as part of a clinical trial."

What are EUI and why is CDC issuing EUI for the COVID-19 vaccine by Pfizer-BioNTech?

In 2013, the Pandemic and All-Hazards Preparedness Reauthorization Act included a new provision that allowed for the issuance of EUI to permit CDC to inform healthcare providers and recipients about certain uses of FDA-approved or cleared medical products. Specifically, EUI inform healthcare providers and recipients about such products' approved, licensed, or cleared conditions of use. The CDC Director has statutory (legal) authority to create, issue, and disseminate EUI before or during an emergency.

The COVID-19 vaccine by Pfizer-BioNTech was approved by the FDA in August 2021 as a 2-dose primary series for active immunization to prevent COVID-19 in persons 16 years of age and older. CDC is issuing these EUI to provide information about use of the COVID-19 vaccine by Pfizer-BioNTech for an additional dose in certain immunocompromised persons aged ≥ 12 years and/or a single booster dose in certain adults aged ≥ 18 years who completed primary vaccination with **non-FDA authorized or approved** COVID-19 vaccines. For example, these EUI cover use of the COVID-19 vaccine by Pfizer-BioNTech in individuals who were vaccinated outside of the United States or in clinical trials with the AstraZeneca COVID-19 vaccine, the Novavax COVID-19 vaccine, or the Sinopharm COVID-19 vaccine, among others.

What is COVID-19?

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that emerged in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from no symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include fever or chills, cough, shortness of breath, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea.

¹ Comirnaty is the proprietary name for the product licensed under the Biologics License Application (BLA). The Pfizer-BioNTech COVID-19 Vaccine has been available since December 10, 2020, pursuant to Emergency Use Authorization (EUA). The originally-authorized Pfizer-BioNTech COVID-19 Vaccine has the same formulation as Comirnaty, and vials of the BLA-compliant vaccine may bear the name "Pfizer-BioNTech COVID-19 Vaccine." Because of these features, and because Comirnaty is commonly referred to as the "Pfizer vaccine" or the "Pfizer-BioNTech COVID-19 Vaccine," these EUI refer to this vaccine as the COVID-19 vaccine by Pfizer-BioNTech.

² A non-FDA authorized or approved COVID-19 vaccine that is listed for emergency use by the World Health Organization, or is included in CDC's [Technical Instructions for Implementing Presidential Proclamation Advancing Safe Resumption of Global Travel During the COVID-19 Pandemic](#) and [CDC's Order](#), or that is a non-placebo part of a clinical trial within or outside the United States that is a WHO-EUL COVID-19 vaccine or a vaccine that is not listed for emergency use by WHO but for which a U.S. data and safety monitoring board or equivalent has independently confirmed efficacy in the United States (hereinafter "non-FDA authorized or approved COVID-19 vaccines").

Who can receive an additional primary dose or a single booster dose of the COVID-19 vaccine by Pfizer-BioNTech ?

- Certain moderately and severely immunocompromised persons aged ≥ 12 years who completed a primary series of non-FDA authorized or approved COVID-19 vaccines are eligible to receive a single additional primary series dose of the COVID-19 vaccine by Pfizer-BioNTech.
- Certain adults aged ≥ 18 years who have completed a primary series of a non-FDA authorized or approved COVID-19 vaccine are eligible to receive a single booster dose of the COVID-19 vaccine by Pfizer-BioNTech.

Refer to CDC's [Interim Clinical Considerations](#) for additional information on moderately and severely immunocompromised persons recommended for an additional primary series dose, populations recommended for a booster dose, and information on non-FDA authorized or approved COVID-19 vaccines included in the recommendations.

What is the dose and interval of the COVID-19 vaccine by Pfizer-BioNTech for an additional primary dose?

A single additional primary dose of the Pfizer-BioNTech vaccine (30 mcg in 0.3 mL) should be administered intramuscularly to certain persons aged ≥ 12 years at least 28 days after completion of primary vaccination with non-FDA authorized or approved COVID-19 vaccines.

What is the dose and interval of the COVID-19 vaccine by Pfizer-BioNTech for a booster dose ?

A single booster dose of the COVID-19 vaccine by Pfizer-BioNTech (30 mcg in 0.3 mL) may be administered intramuscularly to certain adults aged ≥ 18 years of age and older at least 6 months after completion of primary vaccination with non-FDA authorized or approved COVID-19 vaccines.

What are the formulations of the COVID-19 vaccine by Pfizer-BioNTech that these EUI apply to?

The approved COVID-19 vaccine by Pfizer-BioNTech is available in multiple dose vials with purple caps. It is formulated to provide, after dilution, 0.3 mL doses (each containing 30 μ g modRNA). An identical formulation of the vaccine is also authorized by FDA under an Emergency Use Authorization. Like the approved product, it is available in multiple dose vials with purple caps and it is formulated to provide, after dilution, 0.3 mL doses (each containing 30 μ g modRNA). FDA has explained that these products can be used interchangeably to provide doses for the primary vaccination series or booster doses without presenting any safety or effectiveness concerns. Thus, these EUI apply to approved and authorized Pfizer-BioNTech vaccine that is available in multiple-dose vials with purple caps.

What are the common side effects with the COVID-19 vaccine by Pfizer-BioNTech?

Adverse reactions following administration of the vaccine that have been reported in clinical trials and/or post authorization include injection site pain, fatigue, headache, muscle pain, chills, joint pain, fever, injection site swelling, injection site redness, nausea, malaise, lymphadenopathy, decreased appetite, rash, pain in extremity, diarrhea, and vomiting.

What are possible serious side effects with the COVID-19 vaccine by Pfizer-BioNTech?

Severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema), syncope, myocarditis and pericarditis have been reported following administration of the vaccine outside of clinical trials.

Who should not receive the COVID-19 vaccine by Pfizer-BioNTech?

Do not administer the COVID-19 vaccine by Pfizer-BioNTech to persons with known history of a severe allergic reaction (e.g., anaphylaxis) to a previous dose or any component of the vaccine (see *Contraindications, and Warnings and Precautions* sections in the [Comirnaty](#) package insert or [Full EUA Prescribing Information](#) as well

as CDC's [Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States](#) for additional considerations).

What information should be provided to persons receiving an additional primary and/or booster dose of the COVID-19 vaccine by Pfizer-BioNTech as described in the EUI?

- Provide the [EUI Fact Sheet for Recipients and Caregivers](#).
- Provide a CDC COVID-19 Vaccination Record Card to the recipient or their caregiver with the lot number and date of administration recorded for the additional primary or booster dose of the COVID-19 vaccine by Pfizer-BioNTech.
- Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. For more information, visit: www.cdc.gov/vsafe.

What is the available supporting evidence for use of the COVID-19 vaccine by Pfizer-BioNTech for additional primary or booster doses in people who received a primary vaccination series with non-FDA authorized or approved COVID-19 vaccines?

CDC has not systematically evaluated the safety, immunogenicity, and efficacy of a single dose of the COVID-19 vaccine by Pfizer-BioNTech (as either an additional primary series dose for immunocompromised or as a booster dose) following completion of a non-FDA authorized or approved COVID-19 primary vaccination series. However, unpublished studies of COVID-19 vaccine boosting in the United Kingdom have shown that a third dose of AstraZeneca, Moderna, or Pfizer-BioNTech COVID-19 vaccines successfully boosted immune responses in people who had been primed with two doses of Pfizer-BioNTech or AstraZeneca COVID-19 vaccines approximately 3 months earlier. Levels of binding (IgG) and neutralizing antibodies, including against Delta variant, were generally higher when an mRNA vaccine was used as either a heterologous or homologous boost, or where the AstraZeneca COVID-19 vaccine was used as a heterologous boost after primary vaccination with the Pfizer-BioNTech COVID-19 vaccine (1). Frequencies of local and systemic adverse reactions in the 7 days post booster vaccination were higher with heterologous than homologous boosters and in those aged under 70 years when compared to older recipients. Frequencies of local and systemic adverse reactions were higher when the AstraZeneca COVID-19 vaccine was used to boost those who received primary vaccination with the Pfizer-BioNTech COVID-19 vaccine, when compared with the Pfizer-BioNTech COVID-19 vaccine after either primary vaccination (1).

Additional supporting evidence for use of the COVID-19 vaccine by Pfizer-BioNTech for additional primary or booster doses in people who received a non-FDA authorized or approved COVID-19 primary vaccination series are as follows. An unpublished small, randomized trial in Bahrain found that a third dose of Pfizer-BioNTech COVID-19 vaccine after a 2-dose Sinopharm BIBP COVID-19 vaccine primary series resulted in higher levels of IgG antibodies against the spike-antigen of SARS-CoV-2 (anti-S-IgG) compared to a 3-dose series of Sinopharm BIBP COVID-19 vaccine (2). In a pilot prospective cohort study of healthcare workers (HCWs) from Lebanon, 50 HCWs who received a 2-dose primary series of Sinopharm BIBP COVID-19 vaccine and a single booster dose of Pfizer-BioNTech COVID-19 vaccine had significantly higher anti-S-IgG titers compared to 50 homologous vaccinees (2 primary series doses and 1 booster dose of Pfizer-BioNTech COVID-19 vaccine) (3). A longitudinal study of 41 Thai HCWs who received a 2-dose primary series of Sinovac (CoronaVac) COVID-19 vaccine demonstrated booster antibody responses following either AstraZeneca or Pfizer-BioNTech COVID-19 vaccines, including against the Delta variant (4). Local and systemic reactogenicity was reported to be mild to moderate across studies.

WHO's Strategic Advisory Group of Experts (SAGE) on Immunization has noted that although data are currently limited on the safety, immunogenicity, and effectiveness of heterologous versus homologous additional doses, evolving evidence suggests that use of a heterologous vaccine for an additional dose may be more immunogenic than a homologous series. In its recommendations for an additional dose in certain immunocompromised people and in people aged ≥ 60 years who received Sinopharm BIBP or Sinovac-CoronaVac COVID-19 vaccines as a 2-dose primary series, WHO has advised that countries can consider heterologous additional doses based on supply availability (5-7).

More than 80 countries are using boosters after non-FDA approved or authorized COVID-19 vaccines. Countries such as the United Kingdom (8,9), Canada (10,11), Germany, and France have recommended heterologous dosing, including with use of Pfizer-BioNTech COVID-19 vaccine, for an additional primary series and/or booster dose based on their reviews of available immunological and safety data, as well as the epidemiology of COVID-19 and other contextual factors.

Risk-Benefit of the COVID-19 vaccine by Pfizer-BioNTech Additional Primary or Booster Vaccination for Individuals Described in the EUI

The duration of vaccine-induced protection from primary vaccination with COVID-19 vaccines is unknown. Efficacy data from clinical studies of 2-dose primary series supported benefit of the COVID-19 vaccine by Pfizer-BioNTech in preventing severe COVID-19 and supported its FDA approval. Effectiveness of a booster dose of the COVID-19 vaccine by Pfizer-BioNTech is inferred from immunogenicity data in immunocompromised adults who received a single additional primary dose and adults who received a booster dose following primary vaccination with the Pfizer-BioNTech vaccine or another FDA-authorized COVID-19 vaccine. Available data on the safety or efficacy of a Pfizer-BioNTech vaccine dose after receipt of a non-FDA authorized or approved COVID-19 vaccine are limited. However, based on available information, it appears reasonable to anticipate that known and potential risks of an additional primary dose or booster dose of the COVID-19 vaccine by Pfizer-BioNTech may be outweighed by its likely benefit to enhance or restore protection by the primary vaccination, which might have waned over time. Refer to the CDC's [Interim Clinical Considerations for Use of COVID-19 Vaccines](#) for additional information.

Available Alternatives

Currently, the COVID-19 vaccine by Pfizer-BioNTech is the only FDA-approved vaccine for which EUI provide for a heterologous additional primary or booster dose administration following completion with a primary vaccination of non-FDA authorized or approved COVID-19 vaccines.

Reporting Adverse Event or Medication Errors

The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):

- vaccine administration errors whether or not associated with an adverse event,
- serious adverse events (irrespective of attribution to vaccination),
- cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and
- cases of COVID-19 that result in hospitalization or death.

Complete and submit reports to VAERS online at <https://vaers.hhs.gov/reportevent.html>.

For further assistance with reporting to VAERS call 1-800-822-7967.

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